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REMARKS

Present Claims 2-4, 6, and 8-12 relate to methods for treating a dry eye, comprising ocular administration of an effective amount of a macrolide compound to a subject in need of the treatment of dry eye.

The inventor has surprisingly found that ocular administration of a macrolide compound is effective for the treatment of dry eye. The cited reference contains no disclosure or suggestion of the presently claimed methods. Accordingly, these reference cannot affect the patentability of the present claims.

The rejection of Claims 2-12 [*sic*, Claims 2-4, 6, and 8-12] under 35 U.S.C. § 102(b) in view of U.S. Patent No. 5,770,607 (Honbo et al) is respectfully traversed. Honbo et al discloses aqueous eye drop suspensions of a tricyclo compound, including FK506, and their use for the treatment of *vernal* conjunctivitis as an autoimmune disease in the ophthalmic field. On page 3 of the Office Action, the position is taken that *vernal* conjunctivitis is another name for keratoconjunctivitis, and a printout of a page from [www.my.webmd.com](http://www.my.webmd.com) is cited as support for that assertion.

However, the referenced page from [www.my.webmd.com](http://www.my.webmd.com) does not support the equivalence of *vernal* conjunctivitis and keratoconjunctivitis. Instead, this web page only teaches that “*seasonal* conjunctivitis” and “keratoconjunctivitis, *vernal* (*i.e.*, *vernal* keratoconjunctivitis)” are synonymous. As is well known, the adjective “*vernal*” means “of, relating to, or occurring in the spring.” See, the entry for “*vernal*” from Webster’s Ninth New Collegiate Dictionary, Merriam-Webster, Springfield, MA, p. 1310 (1988) filed herewith.

U.S. Application No.: 09/926,411  
Reply to Office Action dated January 15, 2004

In the case of “*vernal* conjunctivitis” and “*vernal* keratoconjunctivitis,” the term “*vernal*” means that the condition is “a seasonal allergic disorder usually appearing during the spring or warm weather.” *See*, page from [www.my.webmd.com](http://www.my.webmd.com) supplied by the Examiner. Thus, to be precise, “*vernal* conjunctivitis” is a seasonal allergic diseases involving autoimmunity.

In sharp contrast, the term “dry eye” as used in the present invention is defined to mean “a condition wherein lacrimal fluid is less in amount or abnormal in quality, with or without the presence of corneal and conjunctival lesion (Yamada, M. et al., *Folia Ophthalmol. Jpn.*, 43, 1289-1293 (1992)).” *See*, page 1, lines 8-11, of the specification. Thus, the *vernal* conjunctivitis of Honbo et al is a very different disease from the dry eye, which is the target disease of the presently claimed methods.

Accordingly, Honbo et al does not disclose any method for treating dry eye or therapeutic effect on dry eye. Accordingly, this reference cannot anticipate the present claims.

Moreover, there is no teaching in Honbo et al which would suggest that administration of a macrolide compound would be useful for the treatment of dry eye. Accordingly, this reference cannot make the present claims obvious.

For these reasons, the rejection should be withdrawn.

Lastly, Applicant wishes to thank Examiner Azpuru for returning an initialed copy of the Form PTO 1449 filed with the Information Disclosure Statement filed on August 7, 2003. However, Applicant notes that References AA, AB, AC, AD, and AY were not initialed.

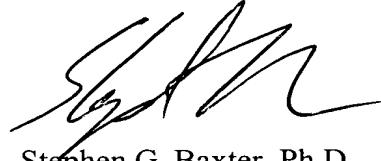
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Since Reference AB was discussed in the Office Action, Applicant presumes that the failure to initial References AA, AB, AC, AD, and AY was simply a clerical error. Accordingly, Applicant is submitting another copy of the Form PTO 1449 filed with the Information Disclosure Statement filed on August 7, 2003, so the Examiner can place his initials next to References AA, AB, AC, AD, and AY and return a copy of the initialed form with the next communication from the PTO.

Applicant submits that the application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

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: the male intromittent organ of any of various invertebrates 2 a : something that borders, limits, or bounds: as (1) : an outer margin of an object or structural part (2) : the edge of roof covering (as tiling) projecting over the gable of a roof (3) Brit : the shoulder of a fowl b : BRINK, THRESHOLD (a country on the ~ of destruction — Archibald MacLeish)

**verge** vi verged; verging (1787) 1 : to be contiguous 2 : to be on the verge or border

**verge vi verged; verging** [L *vergere* to bend, incline — more at WRENCH] (1610) 1 a of the sun : to incline toward the horizon : SINK b : to move or extend in some direction or toward some condition 2 : to be in transition or change

**verger** \vär'jər\ n (15c) 1 chiefly Brit : an attendant that carries a verge (as before a bishop or justice) 2 : a church official who keeps order during services or serves as an usher or a sacristan

**ver-rid-i-cal** \və-'rid-i-kəl\ adj [L *veridicus*, fr. *verus* true + *dicere* to say — more at VERY, DICTION] (1653) 1 : TRUTHFUL, VERACIOUS 2 : not illusory — GENUINE — **ve-rid-i-cal-i-ty** \-,rid-i-'kal-ət-ē\ n — **ve-rid-i-cal-er-ri-able** \vər-i-ə-fi-ə-bəl\ adj (1593) : capable of being verified — **ver-i-fi-abil-i-ty** \vər-i-ə-fi-ə-bil-ət-ē\ n — **ver-i-fi-able-ness** n

**ver-i-fi-ca-tion** \vər-i-ə-fi-ə-kā-shən\ n (1523) : the act or process of verifying: the state of being verified

**ver-i-ify** \vər-i-ə-fi\ vt -fied; -fy-ing [ME *verifiēn*, fr. MF *verifier*, fr. ML *verificare*, fr. L *verus* true — more at VERY] (14c) 1 : to confirm or substantiate in law by oath 2 : to establish the truth, accuracy, or reality of *syn* see CONFIRM — **ver-i-fier** \vər-i-ə-fi\ n

**ver-i-ly** \vər-i-ə-lē\ adv [ME *verraile*, fr. *verray* very] (14c) 1 : in truth : CERTAINLY 2 : TRULY, CONFIDENTLY

**veri-sim-i-lar** \vər-i-sim-i-lər\ adj [L *verisimilis*] (1681) 1 : having the appearance of truth: PROBABLE 2 : depicting realism (as in art or literature) — **veri-sim-i-lar-ly** adv

**veri-sim-i-litude** \vər-i-sim-i-lü-tüd\ n [L *verisimilitudo*, fr. *verisimilis* verisimilar, fr. *veri similis* like the truth] (1603) 1 : the quality or state of being verisimilar 2 : something verisimilar — **veri-si-mil-i-tu-di-nous** \vər-i-sim-i-lü-tüd-nəs, -nəs\ adj

**veri-smi** \vər-i-sim\ n [It. *verismo*, fr. *vero* true, fr. L *verus*] (1892) : artistic use of contemporary everyday material in preference to the heroic or legendary esp. in grand opera — **veri-st** \vəs-t\ n or adj — **veri-stic** \vər-i-stik\ adj

**veri-smo** \vər-i-sə-mō\ n [It.] (ca. 1915) : VERISM: also: REALISM 3

**ver-i-ta-ble** \vər-i-tə-bəl\ adj [ME, fr. MF, fr. *verité*] (15c) : being in fact the thing named and not false, unreal, or imaginary — often used to stress the aptness of a metaphor (a ~ mountain of references) — *syn* see AUTHENTIC — **ver-i-ta-ble-ness** n — **ver-i-ta-bly** \və-təbli\ adv

**ver-i-té** \vər-i-tā\ n [F, truth, fr. MF *verité*] (1966) : the art or technique of filming (as a motion picture) so as to convey candid realism

**ver-i-ty** \vər-i-ə-tē\ n, pl -ties [ME *verite*, fr. MF *verité*, fr. L *veritatis*, fr. *verus* true] (14c) 1 : the quality or state of being true or real 2 : something (as a statement) that is true; esp: a fundamental and inevitably true value (such as honor, love, and patriotism) 3 : the quality or state of being truthful or honest (the king-becoming graces, as justice, ~ —Shak.)

**ver-juice** \vər-jüs\ n [ME *verjus*, fr. MF, fr. *vert jus*, lit., green juice] (14c) 1 : the sour juice of crab apples or of unripe fruit (as grapes or apples); also : an acid liquor made from verjuice 2 : acidity of disposition or manner

**ver-meil** n [MF, fr. *vermeil*, adj. — more at VERMILION] (15c) 1 \vər-mäl, -mäl\ : VERMILION 2 \vər-mäl, -mäl\ : gilded silver — **vermeil** adj

**vermi-** comb form [NL, fr. LL, fr. L *vermis* — more at WORM] : worm (*vermiform*)

**ver-mi-cell-i** \vər-mä-'chel-ē, -sel-\ n [It, fr. pl. of *vermicello*, dim. of *verme* worm, fr. L *vermis*] (1669) : pasta made in long solid strings smaller in diameter than spaghetti

**er-mi-cide** \vər-mä-sid\ n (1849) : an agent that destroys worms

**er-mi-cular** \vər-mä-'mik-yä-lär\ adj [NL *vermicularis*, fr. L *vermiculus*, dim. of *vermis*] (1672) 1 a : resembling a worm in form or motion b : VERMICULATE 2 : of, relating to, or caused by worms

**er-mi-culate** \vər-mä-'lüt\ or **er-mi-culat-ed** \vər-mä-'lät-ēd\ adj [L *vermiculatus*, fr. *vermiculus*] (1605) 1 a : VERMIFORM b : marked with irregular fine lines or with wavy impressed lines (a ~ nut) 2 : TORTUOUS, INVOLUTE 3 : full of worms : WORM-EATEN — **er-mi-cu-la-tion** \vər-mä-'lät-ēshən\ n

**er-mi-cu-lite** \vər-mä-'mik-yä-'lit\ n [L *vermiculus* little worm] (1824) : any of various micaceous minerals that are hydrous silicates resulting usu. from expansion of the granules of mica at high temperatures to give a lightweight highly water-absorbent material

**er-mi-form** \vər-mä-'fɔrm\ adj [NL *vermiformis*, fr. *vermi-* + *-formis* form] (ca. 1730) : resembling a worm in shape

**er-mi-form appendix** n (ca. 1778) : a narrow blind tube usu. about three or four inches long that extends from the cecum in the lower right-hand part of the abdomen

**er-mi-fuge** \vər-mä-'fijū\ adj [prob. fr. (assumed) NL *vermifugus*, fr. *vermi-* + L *fugare* to put to flight — more at -FUGE] (1697) : serving to destroy or expel parasitic worms: ANTHELMINTIC — **vermifuge** n

**er-mil-ion** also **ver-mil-ion** \vər-'mil-yən\ n [ME *vermilion*, fr. OF *vermeillon*, fr. *vermeil*, adj., bright red, vermilion, fr. LL *vermiculus* termes, fr. L, little worm] (14c) 1 : a bright red pigment consisting of mercuric sulfide; broadly: any of various red pigments 2 : a variable color averaging a vivid reddish orange

**er-min** \vər-mən\ n, pl **vermin** [ME, fr. MF, fr. (assumed) L *vermin-*, *vermen* worm; akin to L *vermis* worm — more at WORM] (14c) 1 : a small common harmful or objectionable animals (as lice or fleas) that are difficult to control 2 : birds and mammals that prey on game 2 : an offensive person

**er-minous** \vər-mə-nəs\ adj (1616) 1 : consisting of or being vermin NOXIOUS 2 : forming a breeding place for or infested by vermin

**FILTHY** (as ~ garbage) 3 : caused by vermin (as ~ disease)

**er-mouth** \vər-'mooth\ n [F *vermout*, fr. G *wermut* wormwood, fr. OHG *vermuota* — more at WORMWOOD] (1806) : a dry or sweet aperitif wine flavored with aromatic herbs and often used in mixed drinks

**er-nac-u-lar** \vər-'nak-yä-lär\ adj [L *vernaculus* native, fr. *verna* slave born in his master's house, native] (1601) 1 a : using a language or dialect native to a region or country rather than a literary, cultured, or

foreign language b : of, relating to, or being a nonstandard or substandard language or dialect of a place, region, or country c : of relating to, or being the normal spoken form of a language 2 : applied to a plant or animal in the common native speech as distinguished from the Latin nomenclature of scientific classification 3 : of, relating to, or characteristic of a period, place, or group; esp : of, relating to, or being the common building style of a period or place — **ver-nac-u-lar-ly** \vər-nä-kyü-lär-ē\ adv

**vernacular** n (1706) 1 : a vernacular language, expression, or mode of expression 2 : the mode of expression of a group or class 3 : a vernacular name of a plant or animal

**ver-nac-u-lar-ism** \vər-nä-kyü-lär-izəm\ n (ca. 1846) : a vernacular word or idiom

**ver-nal** \vər-nəl\ adj [L *vernalis*, alter. of *vernus*, fr. *ver* spring; akin to Gk *ear* spring] (1534) 1 : of, relating to, or occurring in the spring (< equinox) (< ~ sunshine) 2 : fresh or new like the spring; also: YOUTHFUL — **ver-nal-ly** \vər-nəl-ē\ adv

**ver-nal-iza-tion** \vər-nəl-iz-ə-shən\ n (ca. 1932) : the act or process of hastening the flowering and fruiting of plants by treating seeds, bulbs, or seedlings so as to induce a shortening of the vegetative period — **ver-nal-ize** \vər-nəl-iz\ vt

**ver-na-tion** \vər-nä-shən\ n [NL *vernatio*, fr. L *vernatus*, pp. of *vernare* to behave as in spring, fr. *vernus* vernal] (1793) : the arrangement of foliage leaves within the bud

**Ver-ner's law** \vətər-nər-zəs\ n [Karl A. Verner] (ca. 1892) : a statement in historical linguistics: in medial or final position in voiced environments and when the immediately preceding vowel did not bear the principal accent in Proto-Indo-European, the Proto-Germanic voiceless fricatives f, þ, and χ derived from the Proto-Indo-European voiceless stops p, t, and k and the Proto-Germanic voiceless fricative s derived from Proto-Indo-European s became the voiced fricatives b, ð, g, and z represented in various recorded Germanic languages by b, d, g, and r

**ver-nic-le** or **ver-na-cle** \vər-ni-kəl\ n [ME *vernicle*, fr. MF *veronique*, *vernicle*, fr. ML *veronica*] (14c) : **VERONICA**

**ver-ni-er** \vər-nē-ər\ n [Pierre Vernier] (ca. 1766) 1 : a short scale made to slide along the divisions of a graduated instrument for indicating parts of divisions 2 a : a small auxiliary device used with a main device to obtain fine adjustment b : any of two or more small supplementary rocket engines or gas nozzles on a missile or a rocket vehicle for making fine adjustments in the speed or course or controlling the attitude — called also *vernier engine*

**vernier** adj (1788) : having or comprising a vernier

**vernier caliper** n (ca. 1876) : a measuring device that consists of a main scale with a fixed jaw and a sliding jaw with an attached vernier

**ver-nis-sage** \vər-ni-'säzh\ n [F, day before an exhibition opens reserved for artists to varnish and put finishing touches to their paintings, lit., varnishing, fr. *verniss* varnish — more at VARNISH] (1926) : a private showing or preview of an art exhibition

**ver-ron-i-ca** \vər-rän-i-kə\ n [NL, genus of herbs] (1527) : SPEEDWELL

**veronica** n [ML, fr. *Veronica* St. *Veronica*] (1700) : an image of Christ's face said to have been impressed on the cloth that St. Veronica gave him to wipe his face with on the way to his crucifixion; also : a cloth resembling the legendary one of St. Veronica

**veronica** n [Sp *verónica*, fr. St. *Veronica*] (1926) : a pass in bullfighting in which the cape is swung slowly away from the charging bull while the matador keeps his feet in the same position

**Vé-ro-nique** also **Ve-ro-nique** \vā-rō-'nēk\ adj [F *Véronique* *Veronica*] (1927) : prepared or garnished with usu. white seedless grapes (sole ~)

**ver-ru-ca** \vər-'rū-kə\ n, pl -cae \-(ə)kē, -ki, -sī\ [L — more at WART] (1565) 1 : a wart or warty skin lesion 2 : a warty elevation on a plant or animal surface

**verru-ca vul-ga-ri-s** \vər-rū-kə-'vəl-gər-əs, -'ger-\ n [NL, lit., common *verruca*] (ca. 1903) : WART la

**ver-ru-co-se** \vər-rū-kō-kōs\ adj (1686) : covered with warty elevations

**ver-sal** \vər-səl, 'vär-səl\ adj [short for *universal*] archaic (1592) : ENTIRE, WHOLE (as pale as any clout in the ~ world — Shak.)

**ver-sant** \vər-sənt\ adj [L *versant*, *versans*, pp. of *versare*, *versari* to turn, occupy oneself, meditate] (1645) 1 archaic: EXPERIENCED, PRATICED 2 : CONVERSANT

**ver-sant** \vər-sənt, ve(sə)r-sənt\ n [F, fr. MF, fr. pp. of *verser* to turn, pour, fr. L *versare* to turn; fr. its shedding of water] (1851) 1 : the slope of a side of a mountain chain 2 : the general slope of a country : INCLINATION

**ver-sa-tile** \vər-sə-təl, esp Brit -sə-til\ adj [F or L; F, fr. L *versatilis* turning easily, fr. *versatus*, pp. of *versare* to turn, fr. *versus*, pp. of *verte*] (1605) 1 : changing or fluctuating readily : VARIABLE (as ~ disposition) 2 : embracing a variety of subjects, fields, or skills; also: turning with ease from one thing to another 3 a (1) : capable of turning forward or backward : REVERSIBLE (as ~ toe of a bird) (2) : capable of moving laterally and up and down (< ~ antennae) b of an anther: having the filaments attached at or near the middle so as to swing freely 4 : having many uses or applications (< ~ building material) — **ver-sa-tile-ly** \vər-sə-tēlē, -til-lē\ adv — **ver-sa-tile-ness** \vər-sə-tēs, -til-nəs\ n

**ver-sa-ti-ly** \vər-sə-təl-ət-ē\ n (ca. 1755) : the quality or state of being versatile (a writer of great ~)

**vers de so-ci-é-té** \vətər-də-sō-sē-ə-tē\ n [F, society *verse*] (1803) : witty and typically ironical light *verse*

**verse** \vərs\ n [ME *vers*, fr. OF & OE; both fr. L *versus*, lit., turning, fr. *versus*, pp. of *verte* to turn — more at WORTH] (bef. 12c) 1 : a line of metrical writing 2 a (1) : metrical language (2) : metrical writing distinguished from poetry esp. by its lower level of intensity (3) : POETRY 2 b : POEM c : a body of metrical writing (as of a period or country) 3 : STANZA 4 : one of the short divisions into which a chapter of the Bible is traditionally divided

**verse vb versed; vers-ing** vi (bef. 12c) : to make verse : **VERSIFY** ~ vi 1 : to tell or celebrate in verse 2 : to turn into verse

**verse vi versed; vers-ing** [back-formation fr. *versed*, fr. L *versatus*, pp. of *versari* to be active, be occupied (in), pass. of *versare* to turn, fr. *versus*, pp.] (1673) : to familiarize by close association, study, or experience (versed himself in the theater)

**vers-et** \vərs-ət-, -et; vər-'set\ n [ME, fr. OF, dim. of *vers* *verse*] (13c) : a short *verse* esp. from a sacred book (as the Koran)